Remarks

Heparin is administered parenterally in vascular surgery and in the treatment of postoperative thrombosis and embolism. Approximately 1% to 30% (average: 5%) of patients receiving heparin have an immunologic reaction resulting in heparin induced thrombocytopenia (HIT). These adverse events may develop into heparin induced thrombocytopenia and thrombosis syndrome (HITTS). Applicants' invention is the first to describe a treatment of HIT with protein C, human protein C zymogen, or human activated protein C.

Claims 11 through 17 are pending in this case. These claims have been cancelled. New claims 18 through 21 are submitted for review. Basis for these amendments may be found in the specification, for example at p. 8, lines 5 through 23; p. 7, lines 26 through 29; p. 16, lines 21 through 23; and p. 6, lines 16 through 23. Applicants assert that no new matter has been added by way of the amendments. Entry of the above amendments is requested.

Rejection of Claims 11-17 Under 35 U.S.C § 103(a)

Claims 11 through 17 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Drohan et al. (US 5,589,604) or Lubon et al. (US 5,831,141). While Applicants do not acquiesce to the merits of this rejection, in order to advance prosecution, the claims are now amended to include the time duration for the human activated protein C dose. This change directs the claims to be defined in terms of the total amount of human activated protein C administered to the human patient by providing a dosage in units of μg/kg/hr along with the time of administration. The lowest possible total human activated protein C amount encompassed by Applicants' claims (20 μg/kg/hr for 96 hours calculated for an average human weighing 70 kg = over 134 mg of aPC) exceeds the total estimated dose per treatment of 10 to 100 mg for thrombolytic therapy noted by Drohan and Lubon as needed to meet the estimated U.S. clinical requirements for protein C and activated protein C. It is important to note that Drohan's and Lubon's total estimated dose is listed in each patent in a table described as containing "data [that] are necessarily based on an incomplete assessment of the therapeutic potential for protein C." Indeed, this table is included in these patents merely to illustrate the need to produce more protein C and activated protein C. Nonetheless, Applicants have modified the claims in order to advance prosecution.

This total human activated protein C amount is calculated using an average human weight of 70 kg. Use of the 70 kg average in this calculation is reasonable because this weight is often noted as the average male human weight. (See Freitas Jr., RA, Nanomedicine, Volume I: Basic Capabilities, Table 8.9, Landes Bioscience, Georgetown, TX, 1999.; Durney CH, Massoudi H, lskander MF, et al. Table 5.4, Average weight and height and calculated values of b for prolate spheroidal models of human-body types, Radiofrequency Radiation Dosimetry Handbook, University of Utah, October 1986.; Boone K, Standard man: average (male) values for various biophysical values. The K-Zone, http://www.kevinboone.com/biodat_stdman.html.) Furthermore, while clinical trials with human activated protein C for HIT and HITTS have not been conducted by Applicants, the average weight of patients with severe sepsis in a clinical trial using human activated protein C was actually slightly higher than 70 kg. (See Bernard GR, Vincent JL, Laterre PF, Larosa SP, Dhainaut JF, Rodriguez AL, et al. Efficacy and safety of recombinant human activated protein C for treatment of patients with severe sepsis. N Engl J Med 2001; 344: 699-709.) This slightly higher average was due to two general reasons: 1) there were more male patients than female patients in these trials and 2) patients were resuscitated with fluid due to their clinical condition. In view of this clinical trial, an average human weighing 70 kg is a more conservative estimate of actual patient weight. Therefore, considering the average male human weight is noted by multiple sources as being 70 kg and the average patient weight in a severe sepsis clinical trial using human activated protein C is slightly higher than 70 kg, utilizing an average human weight of 70 kg to calculate the total estimated human activated protein C dose provided by Applicants' claims is reasonable. Based upon all of the aforementioned points, Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

Applicants assert that the above-stated remarks obviate the noted rejections. In view of these points, Applicants courteously solicit reconsideration of these rejections and passage of this case to issuance.

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